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PATENT

REMARKS

The claims pending are claims 1, 2, and 4-14 are now pending. Claims 3, 11, and 15-20 stand canceled.

Applicants further affirm the correctness of the inventive entity in view of the cancellation of claims.

Applicants respectfully request that the examiner enter the amendment to claim 1, presented above, which is supported in the original specification at page 86, line 7 through page 87, line 32. No new matter is introduced by this amendment.

Applicants make the above amendment in an earnest attempt to further prosecution and obtain allowable subject matter in this application. Any subject matter cancelled from these claims by amendment is reserved for further prosecution in a continuation application filed during the pendency of this application.

Miscellaneous Matters

Applicants wish to draw the Examiner's attention to a Supplemental Information Disclosure Statement, filed by hand with the USPTO on March 31, 2003 and a Revocation of Power/New Power filed by mail on April 9, 2003. Neither document is acknowledged by the Examiner on the Office Action Summary attached to the Office Action of May 1, 2003.

Applicants request that the Examiner advise Applicants of the receipt or lack thereof by the Examiner. Applicants will supply the Examiner with copies of same if the Examiner has never received these documents. If the Examiner received them after transmission of this Action, Applicants request that the Examiner acknowledge receipt and consideration of same in another paper in this prosecution.

Rejections Under 35 USC §103(a)

Claims 1-2 and 4-14 stand rejected under 35 USC §103(a) as being unpatentable over the following combination of documents:

- (1) International Patent Publication No. WO99/67368 (Cases)
- (2) International Patent Publication No. WO97/45439 (Sturley)
- (3) US Patent No. 5,801,154 ("Baracchini"), and
- (4) Fritz et al, 1997 J. Coll. Interface Sci., 195:272-288 (Fritz).

The examiner states that one skilled in the art would have been motivated to make antisense oligos targeted to acyl Co-A cholesterol acyltransferase-2 (ACAT-2), given the teaching of the ACAT-2 sequence by Sturley, the suggestions by Cases and Sturley that antisense sequences to ACAT-2 may be useful; the teaching by Baracchini that antisense sequences can hybridize to a coding region of a gene and the teachings by Fritz that modified oligonucleotides are useful in preference to native sequences.

Applicants respectfully request reconsideration and withdrawal of this rejection in view of the above amendments to the claims and the following remarks.

In view of the submitted amendment to claim 1, the claims now are limited to those antisense sequences that not only hybridize within the sequence of SEQ ID NO: 3 and inhibit expression of the ACAT-2 protein, but do so at a minimum inhibition level of 40%. This amendment, which is amply supported by the specification, which demonstrates at least 15 examples of antisense sequences falling within the claim, is nowhere suggested by any combination of the cited references.

Nothing in Cases or Sturley's unsupported suggestion that antisense sequences to ACAT-2 may be desirable, nor Baracchini or Fritz' generic teachings of modifications to antisense sequences to MRP or other unrelated proteins

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teaches or suggests **any** preferred minimum inhibition of ACAT-2 expression by antisense sequences to ACAT-2. None of these references, taken alone or together supports an inhibition level of ACAT-2 expression of **40%**. None of these references, taken alone or together, provides any evidence that any antisense sequences to ACAT-2 are even capable of providing any desired level of inhibition to ACAT-2.

As demonstrated by Applicants, there are "antisense" sequences that may hybridize to the to ACAT-2 coding sequence, but that provide no inhibition at all or that provide only low levels of inhibition. See, Table I. Therefore, a general reference to the desirability of antisense sequences in Cases and/or Sturley does not provide sufficient teachings to suggest the present invention. Since the modifications suggested by Baracchini and Fritz are only generic comments, or teachings directed to MRP, these references also do not provide the necessary teachings to suggest the presently claimed invention. Nothing in these references points to antisense sequences of ACAT-2 that are capable of generating at least 40% inhibition vs. sequences that generate lesser or no inhibition of expression.

Further with regard to these combined references suggesting that antisense sequences to ACAT-2 are desirable, this is simply a suggestion that it may be obvious to try to obtain such sequences. An obviousness rejection cannot be made by combining documents to make the bald suggestion that it is "obvious to try" to make antisense compounds to target ACAT-2, simply because others have made antisense compounds to other **unrelated** proteins and that antisense sequences to ACAT-2 would be desirable, if made. The US patent law has long held that the "obvious to try" standard is not the appropriate standard for a determination of patentability.

Further, the mere fact that the prior art may be modified in the manner suggested by the examiner does not make the modification obvious, unless the prior art

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suggested the desirability of the modification. As discussed above, the prior art references in combination and taken as a whole do not suggest the claimed invention.

The combination of these references does not provide any expectation of success that if one did target the specifically claimed ACAT-2 SEQ ID NO: 3 sequence of the present claims, that one would obtain antisense sequences with the desired 40% inhibitory result. The only source of the required motivation to make and use antisense compounds capable of inhibiting ACAT-2 expression by at least 40% is provided by the Applicants' own specification. The only teachings that supply the necessary motivation and expectation of success that such a composition would be useful are provided by the instant specification.

In view of the above amendments and these remarks, Applicants' respectfully request that the examiner withdraw the outstanding rejections and permit the above pending claims to pass to issue in due course.

The Director is hereby authorized to charge any additional fees required with the filing of this paper or credit any overpayment in any fees to our deposit account number 08-3040.

Respectfully submitted,

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